Echocardiography and Pulmonary Embolism

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Abstract

Echocardiography is a useful prognostic and diagnostic tool in the management of acute pulmonary embolism. Qualitative and quantitative signs of right ventricular enlargement and dysfunction are essential for risk stratification of patients with acute pulmonary embolism. With the advancement of point-of-care cardiac ultrasound, bedside cardiac ultrasound can be employed in the rapid evaluation of unstable or undifferentiated patients with signs and symptoms of pulmonary embolism. Features associated with high mortality, such as clot-in-transit and a patent foramen ovale are diagnosed with echocardiography. More recently, echocardiographic assessment of cardiac output can help identify normotensive patients in subclinical obstructive shock. Acute and chronic pulmonary embolism may be ascertained with specific echocardiographic features such as the 60/60 sign and the right ventricular wall thickness. Newer echocardiographic techniques such as right ventricular longitudinal strain imaging and three-dimensional echocardiography have been developed but are not yet available ubiquitously. Echocardiography is also employed in practice to monitor response to treatment and for the development of chronic thromboembolic pulmonary hypertension.

Keywords

APE Acute pulmonary embolism · ACT Acceleration time · CIT Clot-in-transit · CO Cardiac output · FAC Fractional area change · LA Left atrium · LV Left ventricle · LVOT Left ventricular outflow tract · PAH Pulmonary arterial hypertension · PAP Pulmonary artery pressure · PFO Patent foramen ovale · PH Pulmonary hypertension · POCUS Point-of-care ultrasonography · PVR Pulmonary vascular resistance · RA Right atria · RAP Right atrial pressure · RV Right ventricle · RVOT Right ventricular outflow tract · TAPSE Tricuspid annular plane systolic excursion · TRV Tricuspid regurgitation velocity · TRPG Tricuspid regurgitation pressure gradient · TTE Transthoracic echocardiography · TR Tricuspid regurgitation · VTI Velocity time integral

Introduction

Acute venous thromboembolic disease is a common disorder with an overall incidence of approximately 300,000–600,000 a year in the USA with 100,000 deaths per year attributable to acute pulmonary embolism (APE) (Beckman et al. 2010). APE is a heterogeneous disease process with varied clinical outcomes with an overall mortality rate exceeding 10% at 30 days. The most common cause of death within 30 days is right ventricular (RV) failure (Goldhaber et al. 1999). The mainstay of treatment in APE is systemic anticoagulation however even with appropriate treatment, a subset of patients are at high risk for decompensation and death (Sanchez et al. 2008).

Transthoracic echocardiography (TTE) allows for the rapid evaluation and differentiation of major life-threatening cardiopulmonary complications. In patients with APE, echocardiography allows for the assessment of cardiac function, providing clues to hemodynamic instability and can influence management decisions. In this chapter, we will review the vital role of echocardiography in evaluating and managing patients presenting with APE.

Right Ventricular Function and Anatomy

The right ventricle is located behind the sternum and is the most anterior cardiac chamber. It has a complex crescent shape when viewed apically and a triangular shape in the short axis (Fig. 1). The primary function of the RV is to return systemic venous blood to the pulmonary arteries for oxygenation, which is then returned to the systemic circulation through the left ventricle (LV). Under normal conditions, the RV contracts against a low pulmonary vascular resistance (PVR) and afterload, resulting in a low-pressure environment for the right side of the heart. The ventricular pressures typically range from 20 to 30 mmHg during systole and 3–7 mmHg during diastole (Haddad et al. 2008). The RV has thin walls making it relatively compliant but more susceptible to acute increases in afterload (Rudski et al. 2010).

In APE, there is a marked increase in PVR causing RV dilation and systolic dysfunction (Wu et al. 2022). RV dilation leads to bowing of the interventricular septum toward the LV resulting in decreased LV filling, reduction in cardiac output, and decreased coronary perfusion (Bryce et al. 2019). These hemodynamic effects can lead to decompensation and death.

Echocardiography is a rapid, sensitive, and cost-effective method to evaluate both the anatomy and function of the RV in patients with a suspected or confirmed APE. It can be done quickly at the bedside to help identify patients at high risk for adverse effects from APE. However, there are several challenges associated with obtaining an accurate RV assessment including its complex crescent shape, retrosternal location, and the heavily trabeculated myocardium making the endocardial surface difficult to visualize (Haddad et al. 2008; Armstrong and Ryan 2019). To overcome these limitations, it is frequently necessary to acquire multiple views to obtain an accurate evaluation of the RV (Wu et al. 2022).

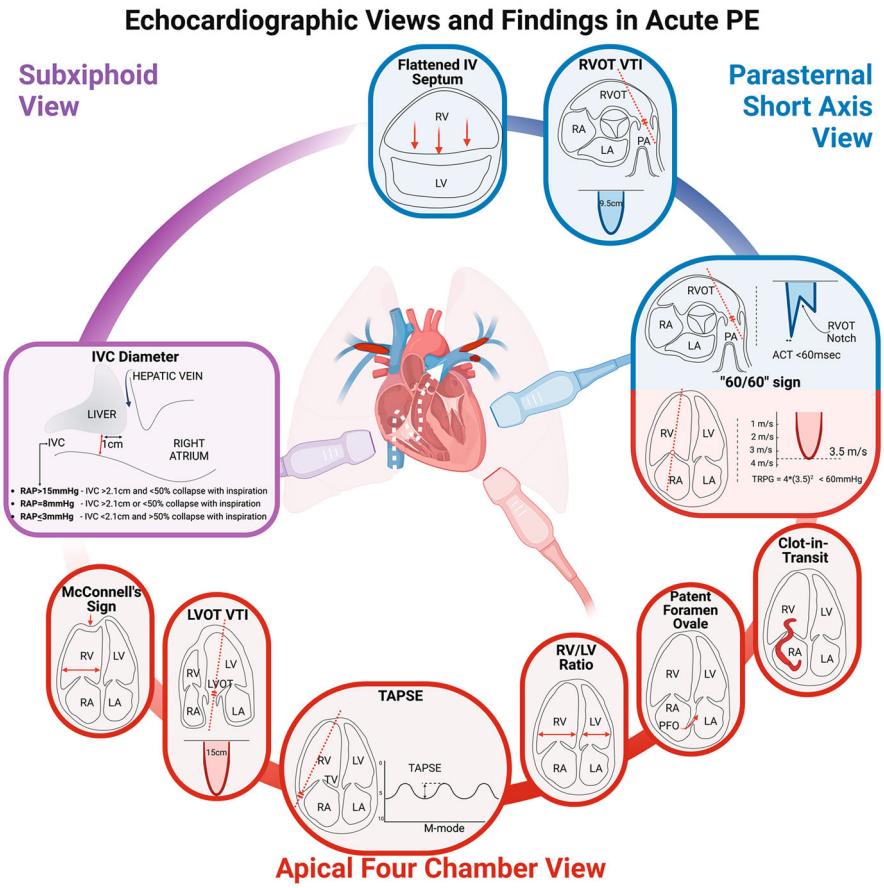

Fig. 1 A pictorial summary of echocardiographic findings in pulmonary embolism. The parasternal short axis view is used to evaluate for IV septal flattening, and the PW Doppler signal of the RVOT. The apical four chamber view is used to assess the TRPG, LVOT VTI, RV/LV ratio, TAPSE, and LVOT VTI and is the best view to evaluate for a McConnell's sign, patent foramen ovale, or clot-in-transit. The subcostal view is used to evaluate the IVC to estimate right atrial pressure. *ACT* acceleration time, *IV* interventricular, *IVC* inferior vena cava, *LA* left atrium, *LV* left ventricle, *LVOT* left ventricular outflow tract, *PA* pulmonary artery, *PFO* patent foramen ovale, *PW* pulse wave, *RA* right atrium, *RAP* right atrial pressure, *RV* right ventricle, *RVOT* right ventricular outflow tract, *TAPSE* tricuspid annular systolic exertion, *TRPG* tricuspid regurgitation valve gradient, *TV* tricuspid valve, *VTI* velocity time integral

Point-of-Care Cardiac Ultrasonography

Point-of-care ultrasonography (POCUS) is defined as ultrasonography brought to the patient and performed by the provider in real time (Moore and Copel 2011). The American Society of Echocardiography and the American College of Emergency

Physicians in a consensus statement describe the importance of the focused cardiac ultrasound as a time-sensitive evaluation of a symptomatic patient (Labovitz et al. 2010). Focused Cardiac ultrasound has also been referred to as cardiac POCUS and bedside echocardiography. Patients who present with cardiac trauma, hypotension, in cardiac arrest, with chest pain or dyspnea should undergo a cardiac POCUS exam. The goals of the focused cardiac POCUS exam are to (1) Assess for the presence of pericardial effusion, (2) Assess the global systolic cardiac function, (3) Identify marked right ventricular or left ventricular enlargement, and (4) Assess volume status by IVC evaluation (Labovitz et al. 2010). Cardiac POCUS is often combined with other symptom-based POCUS exams or multi-system ultrasound protocols such as those for patients presenting with undifferentiated hypotension and shock.

A bedside echocardiogram is recommended as the first line diagnostic study for patients with hypotension who are suspected of having PE (Konstantinides et al. 2019; Konstantinides et al. 2020). Additional POCUS studies such as bilateral lower extremity venous compression ultrasound and in the intubated patient a trans-esophageal echocardiography can be diagnostic. At the bedside, physicians utilize cardiac POCUS to evaluate right ventricular size and function including: right ventricular cavity size relative to the left ventricle, signs of right ventricular overload (presence of McConnell's Sign, flattening of the interventricular septum, dilated non-collapsible IVC), right ventricular longitudinal shortening (tricuspid annular systolic plane excursion), and right ventricular contractility (fractional area change) (Andrus and Dean 2013; Prada et al. 2022). Intra-cardiac thrombus, or clot-in-transit is also visible on cardiac POCUS. Each of these findings, among others will be addressed in this chapter.

Right Ventricular Size

Acute occlusion of the pulmonary arterial bed by thromboemboli, chemical mediator release, and hypoxic vasoconstriction in the affected lung, leads to increased pulmonary vascular resistance (PVR) (Smulders 2000; Lankhaar et al. 2006). The acute rise in PVR leads to right ventricular dilation which can be appreciated in the transthoracic subcostal four-chamber view and in the parasternal long axis view as an enlargement of the RV outflow track (Fig. 1). The apical four-chamber view is used to assess the RV size and ratio of size in comparison to the LV where the LV is larger than the RV in normal conditions. To measure the RV diameter, a modified RV-focused apical four-chamber view is utilized to measure the RV end-diastolic diameter at the level of the annulus (Fig. 1) (Lang et al. 2015). Quantitative measurements of the RV are taken at the base and mid-ventricle at end-diastole in the RV-focused four-chamber apical view. An RV diameter of $>$41 mm at the base and $>$ 35 mm at the mid-level is abnormal (Table 1). These measurements are not routinely reported by most laboratories. More commonly, the RV will be reported as moderately dilated if it is the same diameter as the LV or severely dilated if it is larger than the LV and the RV constitutes the apex (Table 1).

Table 1 Echocardiographic findings in pulmonary embolism

Right ventricular size[a]			
Quantitative		**Qualitative**	
Normal RV basal diameter [mm]	25–41	Normal	RV < LV area with RV apex basal to LV apex
Basal RV dilation [mm]	> 41	Mildly dilated	Enlarged RV, but RV < LV area
Mid RV dilation [mm]	> 35	Moderately dilated	RV = LV area
RVOT diameter[b] [cm]	> 2.7	Severely dilated	RV > LV area, apex formed by RV
Ventricular function			
Quantitative	**Abnormal**	**Qualitative**	
TAPSE [mm]	< 17	McConnell's sign	
S′ [cm/sec]	< 9.5		
RV FAC [%]	< 35		
RV 3D EF	< 45		
RVOT VTI	< 11 cm		
LVOT VTI	< 18 cm		
Right ventricular overload			
Quantitative	**Abnormal**	**Qualitative**	
TRV_{max}[m/s]	> 2.9	D-sign	
ACT [ms]	< 100	ESN of RVOT PW Doppler	
PASP [mm Hg]	> 35		
mPAP [mm Hg]	> 20		
IVC evaluation			
IVC size [cm]	**Sniff [% collapse]**	**Estimated RAP [mm Hg]**	
< 2.1	< 50	≤3	Normal
< 2.1	> 50	8	Mildly elevated
> 2.1	> 50	8	Mildly elevated
> 2.1	< 50	≥15	Very elevated
Equations			
TRPG [mmHg] = 4 x TRV_{max}^2			
PASP [mmHg] = (4 x TRV_{max}^2) + RAP			
CO [mL/min] = VTI_{RVoT} x $Area_{RVoT}$ x HR			
CO [mL/min] = VTI_{LVoT} x $Area_{LVoT}$ x HR			
m PAP [mmHg] = 4 x (PR peak velocity)^2 + RAP			
PAEDP [mmHg] = 4 x (PR end - velocity)^2 + RAP			
m PAP = (1/3x PASP) + (2/3 x PADP)			

ACT acceleration time, *CO* cardiac output, *EF* ejection fraction, *ESN* early systolic notch, *FAC* fractional area change, *HR* heart rate, *IVC* inferior vena cava, *LV* left ventricle, *LVOT* left ventricular outflow tract, *mPAP* mean pulmonary artery pressure, *PAEDP* pulmonary artery end-diastolic pressure, *PADP* pulmonary artery diastolic pressure, *PASP* pulmonary artery systolic pressure, *PFO* patent foramen ovale, *PR* pulmonary regurgitation, *PW* pulse wave, *RAP* right atrial pressure, *RV* right ventricle, *RVOT* right ventricular outflow tract, *S′* tricuspid annular systolic velocity, *TAPSE* tricuspid annular systolic exertion, *TRPG* tricuspid regurgitation valve gradient, TRV_{max} peak TR velocity, *VTI* velocity time integral

[a]Apical-four chamber view at end-diastole

[b]Parasternal short-axis view

The RV to LV ratio has been measured experimentally in many windows including in the long-axis parasternal view, the apical four-chamber view, the subcostal view, and in the parasternal short-axis view. A multicenter prospective study of consecutive patients with normotensive pulmonary embolism evaluated the short-term prognostic value of right ventricular strain by echocardiography and biomarkers. Right ventricular dysfunction by echocardiography was reported as the RV to LV end-diastolic diameter ratio measured in the long-axis parasternal view. In this cohort, patients with adverse events of all-cause death, clinical decompensation or recurrent symptomatic VTE at 30 days had a higher RV/LV ratio 0.9 [0.7–1.0] compared with those not experiencing such events 0.7 [0.5–0.8] (Sanchez et al. 2010). RV dysfunction as indicated by an increased RV to LV ratio was an independent risk factor for the combined outcome of death, clinical decompensation and recurrent symptomatic VTE, independent of PESI score (Sanchez et al. 2013).

The RV to LV ratio may also be assessed qualitatively, as is often the practice in a cardiac POCUS. A normal RV cavity size is less than or equal to two-thirds the size of the left ventricular cavity with the left ventricle forming the apex of the heart. The RV cavity is enlarged if it is equal to or greater than the size of the left ventricular cavity and the apex is formed by the right ventricle (Table 1, Figs. 1 and 2a) (Prada et al. 2022).

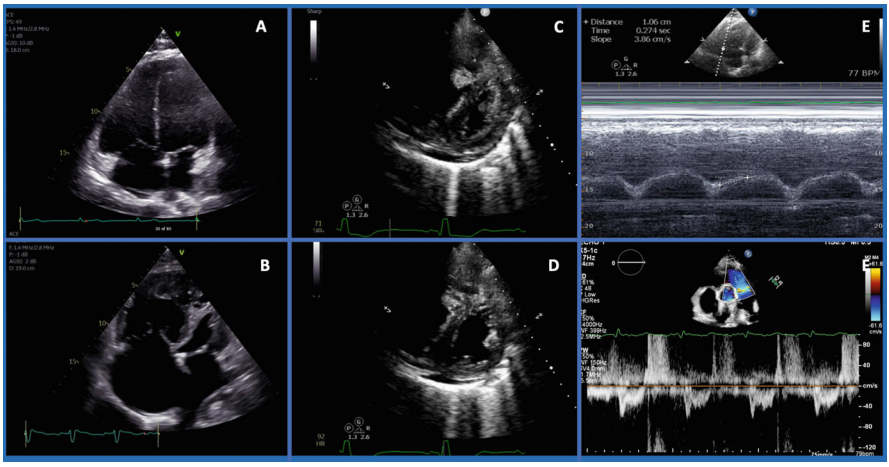

Fig. 2 Echocardiographic features in cases with pulmonary embolism. (**a**) Acute pulmonary embolism and echocardiography finding of a mildly dilated right ventricle at the base, thin right ventricular wall, normal right ventricle base-apex ratio, dilated right atrium, interatrial septal shift from right to left suggestive of elevated right side pressures; (**b**) Chronic pulmonary embolism with evidence of pulmonary hypertension and a severely dilated right ventricle, dilated right atrium, right ventricular hypertrophy, abnormal right ventricle base-apex ratio and interatrial septal shift from right to left suggestive of elevated right side pressures; (**c**) Diastolic septal flattening suggestive of volume overload in the right heart and evidence of pericardial effusion; (**d**) Systolic septal flattening suggestive of pressure overload in the right heart; (**e**) M-Mode measurement of an abnormal tricuspid annular plane systolic excursion less than 1.6 cm; (**f**) Pulse wave Doppler across the RVOT with early systolic notching suggestive of proximal acute pulmonary embolism

McConnell's Sign

McConnell's sign has been described in the setting of APE. It is characterized by akinesis of the RV free wall without the involvement of the apex or base. This finding has a 77% sensitivity and a 94% specificity for the diagnosis of APE, with a positive predictive value of 71% and a negative predictive value of 96% (McConnell et al. 1996). One mechanism for this finding in APE is explained by the tethered RV apex to a contracting and often hyperdynamic left ventricle. When exposed to an abrupt increase in afterload, the RV accommodates by forming a more spherical shape to equalize regional wall stress. The spherical shape combined with systolic contraction corresponds to the bulging of the mid-RV free wall relative to the apex and base. Another mechanism that has been suggested is localized ischemia of the RV free wall due to increased wall stress. The latter suggests that other mechanisms of RV ischemia can also cause a McConnell's sign without PE (Rafie et al. 2022). Thus, the presence of a McConnell's sign should raise high suspicion for APE, but this finding is not pathognomonic.

Septal Flattening

In the parasternal short-axis view, septal flattening can be appreciated in patients with APE. This "D-sign" refers to the D-shaped interventricular septum that is flattened in the setting of RV strain (Fig. 1). Septal flattening during systole will suggest findings of pressure overload such as APE, whereas septal flattening during diastole will imply volume overload (Fig. 2c, d). While septal flattening is reported as an observed finding, the LV deformity has been described quantitively with the eccentricity index which compares the diameter of the LV cavity parallel to the septum (D2) to the diameter of the LV perpendicular to the septum(D1), such that the Eccentricity Index = D2/D1. Under normal conditions, the circular LV has an eccentricity index of 1 in systole and diastole. Among patients with right ventricular pressure overload defined as pulmonary artery systolic pressure of 45 mm Hg or greater, the eccentricity index at end-systole was significantly greater than 1 [1.44 ± 0.16] which distinguished these patients from normal subjects and patients with right ventricular volume overload (Ryan et al. 1985). The eccentricity index is not routinely reported by most laboratories.

Inferior Vena Cava and Right Atrial Pressure

In both acute and chronic PE, right heart failure is a potential consequence of right ventricular pressure overload. As the right heart begins to fail, right atrial pressure (RAP) increases (Sayer and Semigran 2017). This increase in RAP can be estimated by an enlarged inferior vena cava (IVC) with a lack of collapsibility with inspiration (Kircher et al. 1990; Brennan et al. 2007). This relationship is governed by a negative trans-pulmonary pressure gradient at the beginning of inspiration "pulling"

venous return into a relatively non-compliant IVC under higher pressure due to elevated right atrial pressures (Furtado and Reis 2019). It must be noted that patients may have increased IVC size and decreased distensibility due to states such as positive pressure ventilation, cardiac tamponade, or severe tricuspid regurgitation (Levitov et al. 2016).

The IVC diameter is measured 1–2 cm distal from the RA junction in the subcostal view and evaluated for collapsibility after a forceful inspiration or "sniff test." This maneuver requires the patient to quickly inspire in through the nose causing a decrease in intrathoracic pressure and emptying of the IVC into the RA causing collapse of the IVC under normal conditions.

An IVC diameter that measures >2.1 cm and collapses <50% corresponds with an elevated RAP which is estimated at 15 mmHg (Lang et al. 2015; Brennan et al. 2007). If IVC diameter is <2.1 cm and collapses <50% or is >2.1 cm and collapses >50% then the RAP is estimated to be 8 mmHg. If the IVC diameter is <2.1 cm and collapses >50% then the RAP pressure is assumed to be 3 mmHg (Table 1) (Lang et al. 2015). Clinically, IVC collapsibility is known to be a predictor of mortality in patients hospitalized with APE with an OR of 0.23 [0.09–0.53] if the IVC is collapsible >50% (Khemasuwan et al. 2015). Evaluation of IVC size and collapsibility is standard in focused cardiac POCUS (Prada et al. 2022). IVC assessment can be useful in guiding management in patients with APE, as it is not recommended to give a fluid bolus unless the RAP pressure is estimated to be low to prevent further RV dilatation and strain (Konstantinides et al. 2019, 2020).

Clot-in-Transit

Clot-in-transit (CIT) refers to a visualized free-floating clot in the right-sided chambers of the heart and occurs in approximately 4% of patients with APE (Torbicki et al. 2003). CIT is four times more likely to be found in patients with high-risk APE with estimated mortality from 21% to 40% (Casazza et al. 2014). TTE remains the gold standard for the identification of CIT and can be recognized using focused cardiac ultrasound. CITs that are high risk for embolization are typically "snake-like" (Figs. 1 and 3) and highly mobile while clots that line the RA or RV are typically more benign and not associated with VTE (Kronik 1989). Clinical management of CIT remains a topic of investigation and includes anticoagulation alone, thrombolysis, catheter-directed therapies, or surgical embolectomy (Patel et al. 2022).

Right Ventricular Function

Quantitative echocardiographic parameters for RV function are readily obtainable and provide valuable information on function and prognosis. These include tricuspid annular plane systolic excursion (TAPSE), tissue doppler-derived tricuspid lateral annular systolic velocity (S′), right ventricular outflow tract velocity time integral

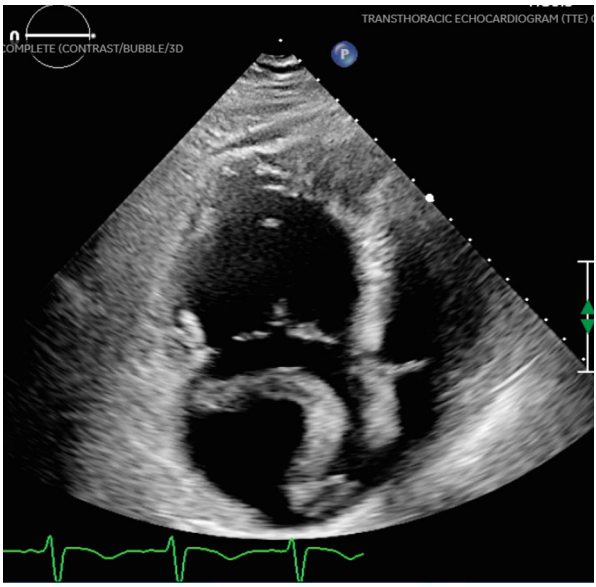

Fig. 3 Clot-in-transit on transthoracic echocardiography in the right atrium is visual as a serpiginous structure that is highly mobile

(RVOT VTI), left ventricular outflow tract velocity time integral (LVOT VTI), RV fractional area change, RV global longitudinal strain, pulmonary artery acceleration time, tricuspid and pulmonic regurgitation, and RV ejection fraction (EF). These measurable parameters, explored in detail below, can be further utilized to calculate hemodynamic function of the right and left ventricle and further prognosticate for patients with APE.

Tricuspid Annular Plane Systolic Excursion

Tricuspid annular plane systolic excursion utilizes M-mode, one of the oldest forms of echocardiography, for its superior temporal resolution. It measures the longitudinal systolic displacement of the right ventricular base, and it is obtained in the apical four-chamber view. To measure TAPSE, the M-mode cursor is aligned along the RV free wall perpendicular to the lateral tricuspid annulus and parallel to the movement of the tricuspid valve annulus (Figs. 1 and 2e). The greater the excursion from the base, the better the RV systolic function. The normal value is $\geq$1.6 cm (Table 1). Overall, TAPSE has low sensitivity and high specificity in distinguishing abnormal from normal function. TAPSE reflects RV longitudinal function with good correlation of parameters estimating RV global systolic function (Forfia et al. 2006). Compared to radionuclide angiography, TAPSE demonstrated an 80% sensitivity and 70% specificity for detecting abnormal RV function (Ueti et al. 2002). TAPSE assumes the motion at the RV base is representative of the function of the entire 3D

RV structure, while some conditions like APE might exhibit regional differences (Rudski et al. 2010).

TAPSE has been shown to have prognostic value in patients with APE. In a prospective study of normotensive patients with APE, TAPSE ≤ to 1.6 cm was associated with an increase in all-cause mortality (Lobo et al. 2014). Another prospective study in normotensive patients with APE showed an increase in 30-day PE-related mortality among patients with TAPSE ≤ to 1.5 cm (Pruszczyk et al. 2014).

M-mode is utilized in a variety of focused cardiac and pulmonary ultrasound protocols, and it has been shown that emergency physicians can accurately obtain this measurement at the bedside (Prada et al. 2022; Karimialavijeh et al. 2022; Duanmu et al. 2020).

Tricuspid Annular Systolic Velocity

Tissue Doppler imaging (TDI) of the tricuspid lateral annular systolic velocity (S′) is another measure of RV systolic function. It utilizes pulsed-wave tissue Doppler at the lateral tricuspid annulus in the apical four-chamber view to measure the longitudinal velocity of excursion. A value <9.5 cm/s indicates RV dysfunction (Table 1). This measurement is less image dependent than TAPSE which requires an optimal axis to accurately quantify maximum annular displacement (Miller et al. 2004). Tricuspid annular systolic velocity has an excellent correlation with RV fractional area change and TAPSE and is a useful measurement to assess RV systolic function in patients with varying degrees of pulmonary hypertension (Saxena et al. 2006).

In patients with APE, both a TAPSE ≤18 mm and S′ ≤ 12.3 cm/s had good positive predictive value and low negative predictive value to predict PE related 30-day mortality or need for rescue thrombolysis, with TAPSE performing slightly better (Kurnicka et al. 2020).

Right Ventricular Outflow Velocity Time Integral and Cardiac Output

The right ventricular outflow tract (RVOT) is best viewed from the left parasternal or subcostal views. In the short-axis view, the diameter of the RVOT should be measured at end-diastole, proximal to the pulmonic valve, from the anterior aortic wall to the right ventricular free wall above the aortic valve. This measurement may be suboptimal if there is poor endocardial definition of the anterior wall. The upper reference limit for the parasternal short axis (PSAX) RVOT diameter is 2.7 cm (Table 1).

Using pulse-wave Doppler at the RVOT, the velocity time integral (VTI) can be obtained which is a value that represents the distance one red blood cell travels. The velocity waveform is traced and the area under the curve is calculated as distance in centimeters (Fig. 1). The stroke volume of the RVOT can be calculated by

multiplying the area (calculated with the measured diameter) times the velocity time integral of the RVOT. Cardiac output (CO) can then be calculated using the echo-derived stroke volume times heart rate. In equation form: $CO = VTI_{RVOT} \times Area_{RVOT} \times$ heart rate (Table 1).

In patients with APE, decompensation and death occur in the setting of RV failure which leads to decreased LV preload and a subsequent drop in cardiac output of the systemic circulation. Accordingly, poor outcomes are seen among patients who demonstrate signs of RV dysfunction on echocardiography. One retrospective study of patients with intermediate-high risk PE requiring invasive therapies found RVOT VTI to be a strong predictor of low cardiac index while RV/LV ratio, IVC diameter, S′, and PASP were not strongly correlated. The study also found that RVOT VTI < 9.5 cm was associated with PE-related mortality (Brailovsky et al. 2019). The utility of RVOT VTI in predicting adverse clinical outcomes in PE patients has been redemonstrated in another retrospective study (Yuriditsky et al. 2020a).

Left Ventricular Outflow Tract Velocity Time Integral and Cardiac Output

The LVOT diameter is best measured in a parasternal long-axis view of the aortic valve in mid-systole. LVOT VTI is measured in the apical five-chamber view using pulsed-wave Doppler in the left ventricular outflow tract proximal to the aortic valve (Fig. 1). The velocity waveform is traced and the area under the curve is calculated as distance (cm). Stroke volume is the area of the LVOT times the distance blood travels at that point. Cardiac output is then calculated by multiplying stroke volume times heart rate: $CO = VTI_{LVOT} \times Area_{LVOT} \times$ heart rate (Table 1).

LVOT VTI is a similar analog of stroke volume and is highly correlated with RVOT VTI.

A retrospective study of intermediate-risk PE patients found that LVOT VTI < 15 cm was associated with in-hospital mortality or cardiac arrest as well as shock or need for reperfusion therapy (Yuriditsky et al. 2020b). In a study comparing the predictors of a composite endpoint of death, cardiac arrest, and hemodynamic deterioration in acute PE patients, the same authors report that low LVOT VTI (< 14.3 cm) outperformed low RVOT VTI (< 10 cm) (Yuriditsky et al. 2020a).

LVOT VTI has been incorporated into emergency ultrasound protocols for patients presenting in shock and thus may be easily acquired by emergency and critical care providers at the bedside as part of a cardiac POCUS exam (Blanco et al. 2015).

Right Ventricular Fractional Area Change

The RV fractional area change (FAC) is a two-dimensional assessment of the RV that is calculated by tracing the RV area, including the apex and lateral wall in systole and diastole, excluding trabeculations. FAC reflects longitudinal and radial components

of the RV contraction. The equation for calculating RV FAC is end-diastolic area—end-systolic area/end-diastolic area × 100. It has been shown to correlate well with RV EF by magnetic resonance imaging (MRI). RV FAC <35% indicates RV systolic dysfunction (Table 1) (Rudski et al. 2010).

Right Ventricular Ejection Fraction

The use of three-dimensional (3D) transthoracic echocardiography provides an integrated view of the interaction of the RV contractility and load, but it is challenging as it depends on the correct acoustic window, rhythm, and interventricular changes (Lang et al. 2015). RV 3D TTE utilizes disk summation and apical rotational methods for RV volume and EF calculations. It correlates well with MRI-derived volumes. There is less underestimation of RV volumes with improved test-retest variability compared to 2D echocardiography. The upper reference limit for indexed RV end-diastolic volume is 89 mL/m^2 and for end-systolic volume is 45 mL/m^2, with volumes 10–15% lower in women compared to men (Rudski et al. 2010). The lower reference limit for RV EF is 44% (Fig. 1). A limitation of 3D TTE is that there is less data available, especially in significantly enlarged or dysfunctional ventricles, making assessment less certain. However, it has prognostic value in acute PE (Rudski et al. 2010).

Tricuspid Regurgitation and Pulmonary Artery Systolic Pressure

Continuous wave Doppler of the tricuspid regurgitant jet is utilized to measure difference in pressure between the right atrium and right ventricle. This measurement may be obtained in the parasternal short-axis, apical four-chamber, or RV-focused view. The tricuspid regurgitant velocity (TRV) is angle dependent so it is important to obtain the highest velocity from multiple views with a dense profile. The modified Bernoulli equation converts the peak TR velocity (TRV_{max}) into pressure to obtain the tricuspid regurgitation pressure gradient: ($TRPG\ [mmHg] = 4 \times TRV_{max}^2$, Fig. 1) (Parasuraman et al. 2016). The TRPG is combined with the estimated central venous pressure (CVP) which is equivalent to the right atrial pressure (RAP) to obtain the right ventricular systolic pressure (RVSP) [mmHg]. The RAP is estimated from IVC size and collapsibility in the subcostal view as discussed previously. Assuming there is no gradient across the RVOT/pulmonic valve such as pulmonic stenosis, the RVSP is equal to the pulmonary artery systolic pressure (PASP). In an equation: $PASP = (4 \times TRV_{max}^2) + RAP$.

A normal peak TR velocity is ≤2.8 m/s, which correlates to an estimated PASP <35 mmHg, assuming a normal RA pressure of 3 mmHg. TRV ≥ 2.9 m/s is considered elevated and suggestive of pulmonary hypertension. Guidelines have recommended the use of peak TR velocity as the key variable for assigning the TTE probability of PH. This method correlates well with invasive measures of PASP on right heart catheterization, which remains the gold standard (Parasuraman et al. 2016).

In patients with severe tricuspid regurgitation, PASP might be underestimated due to early equalization of pressures between the right atrium and ventricle and are more so inaccurate in patients with chronic pulmonary hypertension (Rich et al. 2011). PASP is also related to systemic blood pressure and may be falsely elevated in a patient with hypertension. The use of intravenous contrast or agitated saline sometimes used in echocardiography protocols will overestimate TR velocity and therefore PASP.

Pulmonary Acceleration Time

The pulmonary acceleration time (ACT) can also be measured from the pulse wave Doppler signal used to obtain the RVOT VTI. Mean pulmonary artery pressure is calculated with the pulmonary ACT or from systolic and diastolic PA pressures. In patients with pulmonary hypertension, the pulmonary acceleration has a rapid rise to a peak and therefore a shorter ACT and a higher mean PA pressure (mPAP). The equation for converting acceleration time to mean PA pressure is mPAP [mm Hg] = 90–(0.62 × ACT). A pulmonary ACT > 130 ms is normal, and a pulmonary ACT <100 ms is suggestive of pulmonary hypertension (Table 1). The shorter the ACT, the higher the pulmonary vascular resistance and therefore PA pressure. The invasively measured cutoff for a normal baseline mPAP is 20 mmHg via right heart catheterization.

The RVOT Doppler morphology can also offer insightful information for patients presenting with acute and chronic PE. A normal RVOT Doppler waveform has a hyperbolic shape. Systolic deceleration or "notching" of the RVOT Doppler flow conveys the pathologic wave reflection in the setting of elevated pulmonary artery resistance (Parker et al. 2021). A normal PVR measured invasively is less than two Wood units [WU]. A midsystolic notch would suggest a PVR of 9.2 ± 3.5 Wood's units, whereas a late systolic notch would suggest a PVR of 5.7 ± 3.1 WU (Arkles et al. 2011). In patients with acute massive and submassive PE, an early systolic notch "spike and dome" pattern has been described, which may represent the proximity of the thromboembolism to the pulmonary valve (Figs. 1 and 2f) (Afonso et al. 2019).

Right Ventricular: Pulmonary Artery Uncoupling and the 60/60 Sign

Under physiologic conditions, the RV contractility is relatively matched with the low-pressure pulmonary vascular circulation allowing the transfer of blood to the pulmonary bed. However, in the setting of acute PE, the acute rise in RV afterload causes RV dilation. The resulting chamber enlargement decreases RV contractility, rendering the RV unable to generate adequate systolic pressures (Todaro et al. 2020). This concomitant rise in RV afterload and decrease in RV contractility is known as RV-PA uncoupling. This phenomenon can be demonstrated on echocardiogram with

the "60/60 sign," which is characterized by the presence of a low PASP, estimated by a tricuspid regurgitation peak gradient (TRPG) $\leq$ 60 mmHg, and the presence of low pulmonary ACT $\leq$ 60 ms (Brailovsky et al. 2021).

The 60/60 sign implies that PASP (mmHg) and pulmonary ACT (ms) are both less than 60 suggesting an acute rise in pulmonary vascular resistance. In APE, TRPG $\leq$ 60 mmHg and pulmonary ACT $\leq$ 60 ms had a specificity and positive predictive value of 94% and 90%, respectively (Kurzyna et al. 2002). This finding can be helpful in distinguishing patients with acute PE from those with chronic pulmonary hypertension.

Pulmonary Artery End-Diastolic Pressure and Mean Pressure

The pulmonary artery end-diastolic pressure (PAEDP) and the mean PAP can be estimated by utilizing the pulmonic regurgitant (PR) jet in the PSAX view at the level of the aortic valve.

The PR jet is identified with color Doppler, and continuous wave Doppler is used to obtain the PR signal. The peak PR velocity is used in Bernoulli equation to determine the mean PAP, such that mPAP [mmHg] = 4 (PR peak velocity) (Goldhaber et al. 1999) + RAP (Parasuraman et al. 2016).

The end velocity of the PR jet represents the end-diastolic gradient between the right ventricle and the pulmonary artery. In equation form, PAEDP [mmHg] = 4 $\times$ (PR end-velocity) (Goldhaber et al. 1999) + RAP. The mPAP can also be calculated from the PA systolic and diastolic pressures, mPAP = (1/3 $\times$ PASP) + (2/3 $\times$ PADP) (Table 1).

Right Ventricular Longitudinal Strain

Strain is the percentage change in myocardial deformation and measures regional and global contractility in longitudinal, circumferential, or radial planes (Shah and Solomon 2012). Strain is reported as a percentage [%], with longitudinal and circumferential planes reported as negative values and the radial plane reported as a positive value. Strain evaluation is less dependent on loading conditions compared to volume-based assessments such as of ejection fraction, and visual assessments of myocardial wall motion and thickening. Strain can be evaluated by MRI; however, it is more commonly evaluated with echocardiography given its greater availability. The RV-longitudinal strain is measured in the RV-focused apical four-chamber view. There are two methods for evaluating RV strain, one that measures global strain (GS) and involves all six segments of the RV, and a regional method which focuses on three segments of the RV free wall. RV free wall strain (FWS) excludes the interventricular septum which is argued to be more influenced by LV function. Although the American Society has not recommended reference limits due to high confidence intervals and paucity of data (Rudski et al. 2010). From a study of 238 healthy subjects, the normal range of RV GS was $-24.5\% \pm 3.8$ and RV

FWS −28.5% ± 4.8 (Morris et al. 2017). In a retrospective study, RV FWS was reduced in PE patients compared to healthy controls(−14.4 ± 7.2% vs. −26.0 ± 4.4%, $p < 0.001$) and was the best discriminator between PE and controls when compared to other traditional parameters of RV size and function (Trivedi et al. 2020). RV longitudinal strain is not routinely measured by laboratories, and differences in software algorithms employed by various vendors make comparison of values problematic (Zaidi et al. 2020). More studies on RV strain imaging are needed to understand how this modality can influence the evaluation of patients with APE.

Patent Foramen Ovale

A known sequelae of increased right atrial pressure from PE is increased flow through a patent foramen ovale (PFO), possibly leading to paradoxical emboli including ischemic stroke (Fig. 1) (Kasper et al. 1992). Since the 1990s, it has been known that a PFO found on index TTE in patients with acute hemodynamically significant PE is a strong predictor of mortality [OR 11.4; $p < 0.001$] (Konstantinides et al. 1998). Patients with hemodynamically significant PE and a PFO have been shown to have statistically more ischemic strokes than those without a PFO [13% vs. 2.2%, $p = 0.02$] (Konstantinides et al. 1998). In patients with symptomatic APE, the incidence of PFO was demonstrated to be 13% (Le Moigne et al. 2019). In this cohort of patients, recent ischemic stroke as measured by brain MRI was found to be 21% in the PFO group and only 5.5% in the non-PFO group. While data are lacking regarding echocardiographic diagnosis of PFO specifically in patients with PE, a contrast study with agitated saline is generally accepted as the initial screening tool for PFO with its moderate sensitivity and excellent specificity and should be evaluated in patients with APE and symptoms of stroke. A meta-analysis of 15 studies including 1946 patients demonstrated a sensitivity of 88% [95% CI 77–94%] and specificity of 98% [CI 93–99%] compared to transesophageal echocardiography (TEE) as a gold standard (Ren and Xie 2012). While another large meta-analysis suggests a lower sensitivity of 75% [CI, 66–83%] in finding any right to left shunt as compared to TEE (Khan et al. 2022).

Echocardiography in Chronic Pulmonary Hypertension

Echocardiography provides an assessment of the morphology of the RV and accurately estimates the hemodynamic parameters and signs of RV overload and dysfunction. In cases of pulmonary hypertension (PH) and chronic thromboembolic pulmonary hypertension (CTEPH), there are notable changes that manifest in the right side of the heart and pulmonary vascular bed due to chronic increase in afterload.

Chronic states of pressure overload related to precapillary PH are manifested as RV hypertrophy, RV enlargement and dysfunction, dilation of the tricuspid valve

annulus, tricuspid regurgitation, RA enlargement, dilated coronary sinus, and pericardial effusions. Pulmonary arterial hypertension (PAH), CTEPH, or other causes of precapillary PH cannot be differentiated by echocardiogram but represent sequelae of chronic right ventricular pressure overload (Ghio et al. 2002). Identification of echocardiographic features to differentiate acute vs. chronic conditions will aid the clinician when evaluating APE, as the management of acute and chronic thromboembolic disease is different.

In chronic PE, RV hypertrophy and geometrical remodeling changes occur which are not observed in APE. An increased RV wall thickness (> 5 mm), and increased RV internal diameter and RA dilation can determine the presence of RV hypertrophy (Fig. 2b) (Lang et al. 2015; Baker et al. 1983). The RV wall thickness is best measured by 2DE or M mode at end-diastole preferably in the subcostal view.

In contrast to McConnell's sign, chronic PH causes RV hypertrophy which may limit tethering effects and shape changes, resulting in a more diffuse pattern of RV dysfunction. In chronic PE, the shape of the RV undergoes remodeling as evidenced by a systolic RV base/apex ratio > 2.6 which is suggestive of an elevated PVR >3 WU. The RV base/apex ratio can help discriminate between precapillary and postcapillary PH by echocardiogram (Raza et al. 2017).

In chronically elevated pulmonary artery pressures, a mid-systolic notch can be seen in the RVOT Doppler jet, resulting from transient early closure of the pulmonic valve (Parasuraman et al. 2016). This contrasts with an early systolic notch pattern described previously in APE.

Non-PE Modifiers of Right Ventricle Morphology

In addition to APE, there are several other conditions that may modify the morphology of the right side of the heart. These include RV infarction, obesity, severe metabolic acidosis, acute pulmonary conditions such as acute respiratory distress syndrome, and chronic pulmonary conditions such as chronic obstructive pulmonary disease, interstitial lung disease, hypoventilation syndromes, and sleep apnea. It is important to note that these conditions may be associated with LV diastolic dysfunction, left atrial enlargement, and left ventricular hypertrophy (Freixa et al. 2013).

Conclusion

In addition to diagnostic value, echocardiography in APE can provide prognostic findings which may assist the bedside clinician caring in management decisions. Clinicians caring for patients with pulmonary embolism should be familiar with findings that portend a worse prognosis. Evidence of right heart strain raises suspicion for APE but is not by itself diagnostic. Echocardiography can reveal findings that suggest longstanding elevation of pulmonary pressures from chronic pulmonary embolism and other chronic cardiopulmonary conditions. Cardiac POCUS exams can be performed by trained providers if comprehensive

echocardiography is not immediately available. The limitations of echocardiography are suboptimal cardiac windows, the availability of sonographers and appropriately trained staff. Echocardiography can be used to monitor response to treatment and for long-term follow-up after the index event. Further studies are needed to understand the role of echocardiography including cardiac POCUS to refine and improve risk stratification models and aid clinicians in identifying the patients at highest risk of death and decompensation.

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